CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA
4

KERCKHOFF LABORATORIES
OF BIOLOGY

December 4, 1950

Dr. Joshua Lederberg
Department of Genetics
University of Wisconsin
Madison 6, Wisconsin.

Dear Josh,

Thank you for returning my paper with all the comments. I have submitted it to Genetics, but haven't heard yet what they think of it. If possible, I will try to correct some of the unclear points that you pointed out.

As for the "larmarkian note", here is my line of reasoning : I have concluded, and you tended to agree, that a washed h+ cell is essentially h- before it begins to grow again. A new h+, unlike an old h+ cell, cannot commence to divide on minimal medium unless a small amount of histidine is added. We assume that the new h+, formerly h-, is able to form all amino acids, etc. except histidine. Thus, the (protein) building block essential for the "repair" of the h+ gene which is not already present in the new mutant is histidine. It might be logical to assume that all or many genes in h- or new h+ cells are unable to function effectively with a lack of histidine for substrate. The addition of histidine might make it possible for the activity of many genes to result in the building up of h+ function in the back-mutated gene. Histidine might or might not be one of the building blocks added to the gene, if one may visualize the priming process as the literal building up of genetic material. Histidine, by the way, is reported to be transformed into pyrimidine in bacteria. Thus the entrance of histidine into the gene does not seem to me to be a lamerkian idea in the sense that the gene making histidine is composed mostly of histidine- anyway, I did not mean to imply the latter notion.

Thank you very much for the summary of L&D. What you say about the theoretical clone size varying with the mutation model is certainly true, but I don't see how apparent lag, especially of the magnitude found by Newcombe, could be explained on the basis of any regular type of mutation. I did not attempt to calculate a mean of the Method II data after both you and Newcombe had pointed out the difficulties. The data for Methods I and III were averaged using the number of observations.

You noticed the lack of coherance between the introduction and "cagey" discussion. Actually, I started out with a cagey introduction too, for it is most difficult to come to any conclusions which one can be sure have clear implications for genetics as a whole. However, some of the members of my PhD board wanted the introduction changed, and I had to oblige!

With best wishes,

Peggy [illegible]